# Anion-π Interactions in RNA Tetraloops, A Molecular Mechanics and Quantum Mechanics Approach

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Biological macromolecules rely on various non-bonded interactions to stabilize the 3D conformations which are vital for their structure and functionality. RNA tetra loops are an important structural element in RNA hairpins stabilized by an anion-π interaction between one oxygen anion of a backbone phosphate and the base ring of a neighboring nucleotide (π system). In the present study, we used computational methods, particularly QM calculations and Molecular Dynamics (MD) simulations to sample and measure the anion-π interaction in three RNA tetraloops found in bacterial and human signal recognition particles. Using MD we sampled the anion-π system in its native RNA environment in near-physiological conditions. Mutations that disrupt the anion-π interaction are shown to have distinct dynamics and conformations compared to the wild type tetraloops. We further assessed the effect of RNA-bound proteins on the structure and dynamics of the system. We used QM calculations to assess energetics of structures sampled by MD. We observed that the partners can be anywhere between 2.8Å to 4.4Å from each other and the energy peaks at around -3.8 kcal/mol (bacteria) and -4.3 kcal/mol (human). Mutation of one of the partners will disrupt the interaction and deform the highly conserved tetraloop structure, leading to probable loss of function for the SRP. The protein subunit has significant contribution to the stability of the tetraloop conformation in human SRP as it is directly surrounding the anion-π system and hinders denaturation caused by mutation.